

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>2190 PCT | <b>FOR FURTHER<br/>ACTION</b>  | see Notification of Transmittal of International Search Report<br>(Form PCT/ISA/220) as well as, where applicable, item 5<br>below. |
| International application No.<br>PCT/US03/37081   | International filing date ( <i>day/month/year</i> )<br>10 December 2003 (10.12.2003) | (Earliest) Priority Date ( <i>day/month/year</i> )<br>12 December 2002 (12.12.2002)   |
| Applicant<br>DUKE UNIVERSITY                      |  |   |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☒ **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/37081

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/37081

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/16

US CL : 514/6

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
USPATFUL, CAONLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | US 6,291,424 B1 (STAMLER et al.) 18 September 2001 (18.09.2001), especially abstract.   | 1                     |
| A          | US 6,124,255 A (SCHLAG et al.) 26 September 2000 (26.09.2000), see abstract.  | 1                     |
| A          | JAENIG et al. Uber die Reaktion zwischen Natriumnitrit und Hamoglobin IV. Umsetzung in Abwesenheit von Sauerstoff. Acta Biologica et Medica Germanica (1970), Vol. 25, No. 2, pages 355-358, especially Figure 1. | 1                     |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

|   |  |
|---|--|
| * Special categories of cited documents:  |  |
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "E" earlier application or patent published on or after the international filing date   | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

25 October 2004 (25.10.2004)

Date of mailing of the international search report

03 NOV 2004

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**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim 1, drawn to a first method, a method of making iron nitrosylated hemoglobin comprising reacting deoxygenated hemoglobin and inorganic nitrite.

Group II, claim 2, drawn to a second method, a method of blood product transfusion comprising reacting deoxygenated hemoglobin and inorganic nitrite and transfusing the reacted mixture.

Group III, claim 3, drawn to a third method, a method of blood product transfusion comprising co-infusing a blood substitute or red cells and inorganic nitrite.

Group IV, claims 4 and 5, drawn to a fourth method and a first composition, a method of storing a composition comprising blood, blood substitute, red cells, hemoglobin or mixtures thereof and inorganic nitrite and the composition stored.

Group V, claim 6, drawn to a fifth method, a method of treating a patient in need of nitric oxide therapy.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

An international application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the of following combinations of categories;

- (1) a product and a process specially adapted for the manufacture of said product; or
- (2) a product and a process of use of said product; or
- (3) a product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) a process and a apparatus specifically designed for carrying out said process; or
- (5) a product, a process specially adapted for the manufacture of the said product and an apparatus specifically designed for carrying out said process. 37 CFR 1.475.

The groups of invention fall within category (1), a product and a method of making of that product which are group in Group IV.

Group I is a process of making a product which is not the product of Group IV because Group IV does not require deoxygenated hemoglobin as a starting material.

Group II is a method of use of a product which is not the product of Group IV because the product of Group IV does not require deoxygenated hemoglobin as a starting material and the method of Group II does not require a stored product which is the product of Group IV.

Group III is a method of blood product transfusion which is a co-infusion method and does not require reaction of deoxygenated hemoglobin and inorganic nitrite and does not require a stored product.

Group V is a method of treating a patient in need of NO therapy and does not required the stored product of Group IV and does require deoxygenated hemoglobin as starting material which is not required in the production of the product of Group IV.

# INTERNATIONAL SEARCH REPORT

PC 503/37081

PCT Rule 13 does not provide for multiple methods of use within a single application. Thus, the first appearing composition is combined with a corresponding first method and the additional method claims each constitute a separate group.